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Fehr, Ernst ; Declerck, Carolyn H ; Boone, Christophe ; Pauwels, Loren ; Vogt, Bodo

Abstract: In an influential paper, Kosfeld et al. (2005) showed that intranasal administration of oxytocin (OT) increases the transfers made by investors in the trust game—suggesting that OT increases trust in strangers. Subsequent studies investigating the role of OT in the trust game found inconclusive effects on the trusting behaviour of investors but these studies deviated from the Kosfeld et al. study in an important way—they did not implement minimal social contact (MSC) between the investors and the trustees in the trust game. Here, we performed a large double-blind and placebo-controlled replication study of the effects of OT on trusting behaviour that yields a power of more than 95% and implements an MSC condition as well as a no-social-contact (NoC) condition. We find no effect of OT on trusting behaviour in the MSC condition. Exploratory post hoc analyses suggest that OT may increase trust in individuals with a low disposition to trust in the NoC condition, but this finding requires confirmation in future research.

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A registered replication study on oxytocin and trust

Carolyn Declerck[1], Christophe Boone[1], Loren Pauwels[1], Bodo Vogt[2], Ernst Fehr*[3]

[1] Faculty of Business and Economics, University of Antwerp, Belgium

[2] Chair in Empirical Economics and Health Economics, Otto-von-Guericke-University Magdeburg, Germany

[3] Laboratory for Social and Neural Systems Research, Dept. of Economics, University of Zurich, Switzerland

Corresponding author: Ernst Fehr (ernst.fehr@econ.uzh.ch)

In an influential paper, Kosfeld et al. (2005) showed that intranasal administration of Oxytocin (OT) increases the transfers made by investors in the trust game – suggesting that OT increases trust in strangers. While subsequent studies investigating the role of OT in the trust game found inconclusive effects on the trusting behavior of investors, they deviated from the Kosfeld et al. study in an important way as they did not implement a minimal social contact between the investors and the trustees in the trust game. Here, we will carry out a large double blind and placebo controlled replication study of the effects of OT on trusting behavior that implements the minimal social contact condition and compares it with a no-social-contact condition. The sample generates a power of more than 95% to detect a true effect of OT on trusting behavior in the trust game.

All positive human relationships involve trust, making it one of the most widely-studied topics in the social sciences. To learn more about the biological basis of trust, researchers have investigated the potential causal link with the hormone oxytocin (OT), a neuropeptide with a central role in regulating social approach and attachment behaviors in many non-human mammals[1–3]. In humans, OT is mostly known for its functions in childbirth and breastfeeding, but it can also alleviate social stress, for example, by lowering salivary cortisol levels[4], increasing parasympathetic control of the heart[5], and attenuating amygdala activation in response to seeing faces[6,7]. It is therefore possible that OT could reduce social apprehension between strangers and facilitate trust.

This question has sparked more than a decade of research ever since the first report that administering a single dose of intranasal OT (compared to placebo) increases the willingness to trust in a dyadic economic game with real monetary stakes[8]. In this game, two anonymous players are assigned the role of either an investor or a trustee, and both the investor and the trustee have the same monetary endowment. The investor can transfer money from his endowment to the trustee, knowing that the transferred amount will be multiplied by a factor of three. The trustee, who now enjoys a substantial financial advantage, can honor the investor's decision with a back transfer, thus sharing the proceeds of the investment. When the investor entrusts a large amount and the trustee is fair by sending back, say, 50% of the available amount, both earn a higher income. However, the trustee can also act selfishly and keep everything for himself, making the investor worse off than if he had not trusted at all. The highly interdependent nature of this game thus places the burden of uncertainty on the investor, because the investor does not know how the trustee will respond to his transfers. If

both players are selfish and know that their partner is selfish the investor will transfer nothing because he or she knows that the trustee will maximize self-interest and return nothing. This solution is, however, suboptimal because it reduces the payoffs for both the investor and the trustee relative to what they could have earned if the investor trusts fully and the trustee behaves trustworthily.

Money transfers in the trust game indicate that investors are willing to tolerate a certain level of uncertainty. Interestingly, the worry that another person may not reciprocate appears to influence transfers beyond the perceived riskiness of the game[9,10], i.e., it is not just the risk of losing money but the fear of being cheated (i.e., betrayal aversion) that inhibits the investors' trust. Kosfeld et al.[8] hypothesized that if trust entails overcoming the fear of betrayal in order to attain a profitable interaction, the psychophysiological mechanisms underlying trusting decisions might be similar to those underlying social attachment in other mammals and, therefore, OT might facilitate trusting behavior - a view that is consistent with the results in Kosfeld et al.[8]

Cited more than 1600 times in the Web of Science (and more than 3500 times in Google Scholar, as of August 22, 2018), the Kosfeld et al.[8] study has become a classic reference in both theoretical and empirical studies on human social behaviors, including not only trust, but also social cognition[11-13], empathy[14,15], and group dynamics[16,17]. However, the mounting popularity of studying OT in the social sciences is currently associated with waves of criticism, because papers often have suffered from small sample size, low statistical power, inflated effect sizes, inconsistent experimental procedures, and publication bias[18,19]. Other critics have pointed out that there is no overarching theory to explain the diverse findings resulting from intranasal OT

administration[20]. More specifically, Nave and colleagues[21] have raised doubt on the robustness of the oxytocin-trust association, pointing out that six studies failed to replicate the initial findings reported by Kosfeld et al.[8]. These studies were, however, not direct replications, i. e., they did not use the same methods and procedures as the original study.

To move forward with a research paradigm on the biological basis of trust that includes a role for OT, it is essential to clarify whether OT increases trust, and if so, to establish the conditions under which this is the case. Because animal research has documented that OT is primarily a social bonding hormone that activates socio-emotional neural pathways in the brain[22,23], we would also expect the effect of OT in humans to be limited to social situations where initiating or establishing partnership is important to realize synergy. The Kosfeld et al. study[8] already suggested this: OT increased trusting decisions in the trust game, but did not augment risk-taking in an identically framed risk game played against a computer. To enhance the saliency of the social context, participants in the trust game had some minimal social (face-to-face) contact with each other in groups prior to playing the game against someone whose exact identity would not be revealed. Importantly, the social contact had to be minimal to avoid elevating trust to a level beyond which no further increase could reasonably be expected after OT administration. The following two conditions thus needed to be fulfilled: (i) the social contact took place before participants knew they would play the trust game so that they could not communicate about it, as communication is known to substantially increase cooperation in social dilemma games (such as the trust game)[24]. (ii) Social contact was not intense enough to cause strong feelings of social familiarity, as this might also generate a ceiling effect in trust.

Despite the enormous resonance of the Kosfeld[8] et al. study, the minimal social contact feature of the study has often been overlooked or neglected. In fact, replication studies so far neglected several key features of the trust game played in Kosfeld et al.[8] Of the six studies that entered the meta-analysis in Nave et al.[21] – in addition to the Kosfeld[8] et al. study – four studies had fictional partners[25-28], one was completely devoid of human contact with other participants[29], and participants' previous experience in a dictator game was likely to confound the decision to trust in the sixth study[30]. In this last case, the investor was matched with a partner whom he had been enticed to treat unfairly in an immediately preceding dictator game, which probably altered the investors' beliefs about this partner's trustworthiness. Thus each of the six additional studies in Nave et al.[21] had one or more problematic features.

The importance of establishing some minimal social contact with real partners was corroborated in a large (N = 254) behavioral study[31] in which participants, who did not know each other's identity, needed to trust each other to jointly solve a coordination game. In this two-person simultaneous move game, participants had the choice of playing a safe strategy which ensured a low positive payoff without any (social) risk, but they also could achieve a high, mutually advantageous, payoff if they played the alternative strategy and the partner matched their choice. However, if the partner did not match their choice of the alternative strategy the participants earned much less than what they would have earned under the safe strategy. Thus, the alternative strategy was risky and the players' had to trust that the partner matched their risky choice when playing the alternative strategy.

It turned out that intranasal OT significantly increased coordination on the mutually beneficial alternative strategy, but only if participants first had the opportunity to introduce

themselves to the whole group of participants from which one was randomly drawn to become the partner. Without this prior contact, OT significantly reduced coordination on the alternative strategy.[31] Since the publication of this study, increasing evidence suggests that OT's function is not always consistent with facilitating social approach, but that administering intranasal OT can also lead to parochial, competitive, and envious behaviors and behaviors that appear to be driven by schadenfreude[16,17,32], which have an anti-social dimension. This points to the need of examining the conditions under which – and how – OT modulates social behavior[33,34].

A current leading theory to account for why OT can stimulate both prosocial and anti-social behaviors rests on neurological evidence that OT modulates mesolimbic dopaminergic neurons, thereby affecting both incentive motivation as well as attention re-orienting. By boosting the dopaminergic signal in the mesolimbic network, OT is thought to enhance the salience of social cues that emphasize the value of approach behavior[7,35,36]. Framing the effects of OT in terms of assigning salience to social cues highlights the importance of establishing minimal social contact prior to engaging in an interdependent exchange. We propose that minimal social contact is the cue that enhances the prosocial approach potential of OT and reduces social apprehension, thereby enhancing trust in an environment where approach behavior is a precondition for a mutually advantageous exchange.

The purpose of the proposed study is therefore twofold. First, we want to resolve the conflict regarding the impact of intranasal OT on trusting decisions by conducting a controlled replication experiment of the Kosfeld et al.[8] study with sufficient statistical power. Second, we will investigate the importance of providing social cues by differentiating between a minimal social contact and a no contact environment. Both conditions involve real and anonymous

partners, but differ in the degree to which it is possible to establish minimal social contact: in the minimal contact condition the matched players in the trust game will know that they saw each other while waiting together with several others in a common room (following similar procedures as in Kosfeld et al.[8]), while in the no contact condition the players do not meet and hence have no concrete social cue to relate to each other. To summarize, we propose a 2x2 experimental design with OT versus placebo as the main factors in the first dimension and "no contact" versus "minimal social contact" being the main factors in the second. The primary hypotheses are that OT increases trust in the minimal social contact condition, and that this effect of OT on trust is more pronounced than in the no contact condition. Thus, the proposed design enables us to examine the role of OT for investors' trusting behavior in the trust game and the extent to which this measure of trust is jointly affected by OT and minimal social contact. We believe that these questions are of primary importance for the field of OT research but, naturally, our design does not allow us to make broad conclusions about the general effects of OT on social cognition, empathy or behavior in other experimental paradigms.

Methods

Study sample and determination of sample size

We will conduct the study in two different locations: in Antwerp, Belgium (n = 352) and in Magdeburg, Germany (n = 352) with a total of 704 student participants between 18 and 25 years old. According to the *a priori* power analysis presented in detail below and the robustness check reported in Supplementary Information 1 and 2, a sample size of n = 704 will provide a

153 statistical power of more than 95% for all main hypotheses and also exceeds the sample size
154 recommendations of Nave et al.[21].

155 The sample size for this study is determined based on a series of power analyses in G*Power
156 3.1.9.2 28 and the effects reported in Kosfeld et al.[8]. This paper reported three effects:
157 (i) Comparing a placebo and an OT group in a trust experiment with minimal social contact
158 corresponded to an effect size d = 0.514 (r = 0.249 in a common effect size language).
159 (ii) They compared the OT group in the trust experiment to the OT group in a risk
160 experiment in which they hypothesized OT would not exert an influence. This yielded an effect
161 size of d = 0.701 (r = 0.331), which corresponds to an intermediate effect[37].
162 (iii) To bolster their results, Kosfeld et al.[8] assessed the global difference between all four
163 experimental groups under consideration (trust/Placebo, trust/OT, risk/Placebo, and risk/OT) to
164 ensure a family-wise error of $\alpha = 5\%$. The reported findings correspond to an $\eta^2 = 0.071$ (r =
165 0.267).

166 Kosfeld et al.[8] were forced to use non-parametric tests in their study because their sample
167 did not comply with assumptions made in parametric tests. Specifically, the smallest sample
168 size in testing (i)-(iii) was n=29. They thus applied Mann-Whitney-U tests in (i) and (ii), but
169 implemented Kruskal-Wallis-H for comparison (iii). Our study will overcome these drawbacks
170 because we will recruit a large sample that will enable us to use OLS regression techniques.
171 Given our 2x2 experimental design, the test that would corresponds to (i) compares trust in the
172 minimal social contact condition between the OT and the Placebo group. The test most similar
173 to (ii) compares trust under OT between the no-contact and the minimal social contact
174 condition, and a test similar to (iii) examines whether the trust levels in the four conditions

differ from each other. Note, however, that the tests described in (ii) and (iii) in the Kosfeld study[8] are about comparisons between a *trust* and a *risk* game, which differ substantially from the current design which does not have a *risk* game (i.e., a game played against a computer). Our second factor (minimal social contact versus no contact) establishes variation *within* a trust game played with real partners.

We base our a priori power analysis on the effect size d = 0.514, reported in test (i) of Kosfeld et al.[8] and the requirement of a one-tailed test, which is justified when testing a directional[38] hypothesis. The power analysis shows that with $\alpha = .05$, $\beta = .95$, and a one-tailed t-test we must recruit 166 observation units to detect a significant difference of OT in the minimal contact condition of the proposed experiment (i.e., replicating effect (i), see Supplementary Table 1). Since the proposed experiment will also include a no contact condition, the total necessary sample size is $166 \times 2 = 332$. Because we plan to have 16 participants per session with 22 sessions we will have n = 352 participants per location, which gives us in total n = 704 observations. Based on the reported effect size in result (i) of Kosfeld et al.[8], the overall sample size of n = 704 will provide a statistical power of 99.65%.

However, because of publication bias and other reasons the first results of a study design such as Kosfeld et al.[8] may overstate the true effect size, we conduct a further robustness check in our a priori power analysis by applying Simonsohn's "small telescopes" approach for replication studies[39]. Instead of pondering whether or not it is adequate to assume an effect size of 0.514, the small telescopes approach assesses whether the replication is sufficiently powered so that it is able to detect an effect reported in an original study that may have been "small" or "underpowered". In addition, it differentiates noisy replication effects (yielding p >

.05) from those that genuinely indicate the effect is undetectably different from zero. Specifically, the small telescopes method first ask what effect size d* would give the original study 33% statistical power. Then, in a second step, one computes the number of observations that is necessary to achieve 80% power to detect the relatively small effect size d* in the replication study. According to this method, already an overall sample size of n = 488 yields an adequate replication of the Kosfeld study[8] (see Supplementary Table 2).

Exclusion criteria

We limit recruitment to male participants for several reasons. First, the main motivation for the study is to replicate the Kosfeld et al.[8] study, which was conducted only with males. Second, we know from the previous literature that sex-specific gonadal steroids influence OT-receptor binding in the brain, and that intranasal oxytocin can affect the behavior of males and females differently, even in opposite directions[40]. Such inter-individual differences might introduce excessive noise in the data which could obscure the results. Third, for practical reasons (given that oxytocin induces labor), we wanted to avoid having to administer pregnancy tests to all female participants, which would be required by Ethics Commissions. Finally, in pilot studies (see Supplementary Table 3a) conducted to develop an appropriate minimal social contact condition that avoids ceiling effects, we noted that the gender composition of the social group had a significant impact on subsequent trusting behavior (Supplementary Table 3b).

Other exclusion criteria for participation include (1) psychiatric disorders that may impact the expected effects of OT in healthy populations, and (2) somatic conditions that may impact effective absorption of intranasal OT. To identify psychiatric symptoms, online registration will

include a questionnaire with the following items: (a) Have you ever been diagnosed with a psychiatric disorder? (b) Have you experienced recurrent problems with substance abuse? (c) Are you currently or have you in the past been seeing a psychiatrist, psychologist, or psychotherapist? (d) Do you currently or have you in the past taken psychoactive medication, i.e., sleep medication, anxiety medication, antipsychotics, or antidepressants? If the answer is "yes" to any of these questions, the participant will be contacted by a certified psychologist who will conduct a structured interview to determine if the condition meets diagnostic criteria for psychiatric disorders in DSM-IV. Based on the psychologist's diagnostic report we will consider the following disorders as exclusion criteria for the current study: psychotic disorders or mood disorders with psychotic features; major depressive or (hypo)manic episode; generalized anxiety disorder; panic disorder; agoraphobia or social phobia; obsessive compulsive disorder; alcohol abuse and dependence, and non-alcoholic psycho-active substance use disorder.

To identify somatic conditions, we query participant's history of nasal diseases by (i) asking if participants ever had surgery on the nose and (ii) by administering a standardized and validated questionnaire for subjective assessment of nasal obstruction (NOSE)[41,42]. Participants who have had surgery on the nose or who score in the "severe" range on the NOSE questionnaire[41] are excluded from further data analysis.

Via a post experimental questionnaire, we identify two *post hoc* exclusion criteria: (1) suffering from a common cold or allergic rhinitis on the day of the experiment, which will be assessed subjectively using the standardized Visual Analogue Scale (VAS). The VAS comprises a 10 point scale whereby the extreme cases are given by "nose feels extremely clear," (= 0) and

241 “nose feels extremely blocked.” (= 10). The score on this scale has been shown to correlate
242 specifically with inspiratory flow in the upper nasal cavity[43,44]. Participants who have a score ≥ 8
243 on the VAS are considered to have severe nasal obstruction[43] and will be removed from the
244 data before analyses. We also assess (2) compliance with the online registration instructions to
245 abstain for at least 12 hours from alcohol, non-prescription drugs, and heavy smoking (>20
246 cigarettes) prior to attending the experiment. Because of the anti-diuretic properties of OT, we
247 ask participants to restrict their general consumption of liquids (e.g. water) two hours prior to
248 the experiment to prevent an inadvertent increase of the possibility of water intoxication.
249 Participants who indicate on the day of the experiment that they drank more than one liter in
250 the hour preceding the experiment will not be allowed to self-administer the spray and will no
251 longer be included in the dataset. We will also exclude participants from the dataset based on
252 their answer to specific questions regarding tobacco-, alcohol- and drug use. We will exclude
253 the data of participants who smoked > 20 cigarettes or drank any alcohol on the day of the
254 experiment, and of participants who used non-prescription (recreational) drugs on the day or
255 the night before the experiment. We deliberately collect information about these behaviors
256 immediately after the experiment (i.e., after participants have been paid) so that they have no
257 incentive to lie.
258 A final criterion is participants’ understanding of the trust game instructions. We will check
259 this by letting them compute the monetary payoffs for both players in two hypothetical
260 examples of the trust game. Both examples need to be solved correctly to be included in the
261 data analyses.

Participants will be recruited by e-mail and announcements posted on the university's electronic learning platform (Antwerp), or via an existing participant pool platform (Magdeburg) that introduces the study as "The psychobiological foundations of decision-making". Participation will be voluntary, and all participants will sign an informed consent form. The proposed study will be carried out with the approval of the Medical Ethics Commissions of the Universities of Antwerp and Magdeburg.

Study design

We will test the combined effects of OT and minimal social contact on trust in a 2×2 factorial design (OT/placebo x minimal social contact/no contact), where each treatment is a between factor. Participants' level of trust (the dependent variable) will be assessed with a single decision in a dyadic incentivized trust game (similar to Berg and colleagues[45]). Trust is measured by how many euros participants in the role of the investor are willing to transfer to another participant, the trustee. Measuring trust with a single decision (rather than averaging several consecutive decisions) has the advantage that it prevents hedge betting and may thus encourage intuitive thinking, which is the decision making type OT is most likely to influence,[7,47] rather than complicated deliberation.

The trust game is programmed in z-tree [47], and played on computers linked in a local network. The script will be made accessible via the Open Science Framework. Each person in a dyad is assigned the role of an investor or a trustee. As in Kosfeld et al.[8], both the investor and the trustee receive an initial endowment of 12 euros, and the investor can decide to send 0, 4, 8, or 12 euros to the trustee. The experimenter triples each euro the investor transfers, and this

amount is added to the initial 12 euro endowment of the trustee. Then the trustee has the option of sending back any amount between zero and the total amount available to him. The experimenter does not triple the back transfer. The investor's payoff corresponds to the initial endowment minus the transfer to the trustee, plus the back transfer from the trustee. The trustee's payoff is given by his initial endowment plus the tripled transfer of the investor, minus the back transfer to the investor.

Each participant will play this game twice, with two different partners: first as an investor, and then as a trustee. This ensures that for every investment decision there is also a trustee who decides on a back transfer. The first game in the role of the investor occurs without knowing that there will be a second game in the role of a trustee, and no feedback will be given in between games. In both roles, participants play the trust game for real money.

Participants will be randomly assigned to one of the four treatment conditions (no contact/Placebo, no contact/OT, minimal social contact/Placebo, minimal social contact/OT) but randomization will be stratified based on participants' social value orientation (SVO) which will be measured during registration two weeks prior to the experiment with an online survey. This stratification ensures that the distribution of individuals' SVOs will be the same in each treatment condition. SVO is a relatively stable personality feature describing a person's intrinsic willingness to behave prosocially[48], that has been found to predict trusting decisions[49] and sensitivity to social cues[50]. OT/placebo administration will be double blind following a randomized block design (with a block corresponding to a session).

Spray administration

A recent study investigating the dose dependency of oxytocin reports that a dose of 24 IU OT is more effective in triggering an amygdala response and eliciting fear reduction compared to either lower (12 IU) or higher (48 IU) doses[51], although this contradicts an earlier study in which 8 IU was found to be the most effective[52]. The latter study, however, made use of a Breath Powered device for OT administration which is likely to have increased absorption significantly. Because the aim of the study is to replicate the Kosfeld et al.[8] study as close as possible, we will have participants self-administer 24 IU OT or a placebo by means of a metered finger sprayer (see Supplementary Figure 1). The solutions, containing 1 ml of either syntocinon (Novartis) or an isotonic solution with no active ingredient, are prepared by the pharmacy of the University Hospital pharmacy.

As accumulating evidence suggests that the most likely uptake of intranasal OT into the brain occurs directly via the olfactory or trigeminal nerve (rather than via the circulatory system)[53], participants will receive detailed written and oral instructions (following the guidelines of Guastella et al.[54], see Supplementary Table 4) to make sure that the spray reaches the posterior upper end of the nasal cavity where absorption can take place. All experimenters will train themselves to use the spray bottles properly. During the experimental session we will have a ratio of one supervisor for 4 participants. The supervisor will take notes on any problems participants may be experiencing with the spray and rate whether they properly self-administered the spray on a 5 point likert scale. If participants are rated as non-compliant with the rules for self-administration (category 5) or the self-administration is judged as problematic by the supervisor (category 4) the participant is ruled out from data analysis. Participants

themselves will also report on a 5 point likert scale the discomfort they experienced (if any) from the spray. Scores on this scale will not serve as exclusion criteria, but will be used in further exploratory analyses to assess if nasal spray discomfort might interfere with proper OT administration and affect the behavioral results.

Experimental procedures

Participant recruitment will start at least two weeks prior to the experiment. Registration occurs online and includes filling out the triple dominance measure for social value orientation (SVO)[48;] the inclusive generalized trust scale[49], a measure of risk attitude[55], and two questionnaires assessing attitudes towards social contact (the shortened version of the Autism Spectrum Questionnaire (ATQ10)[56] and the sociability dimension of the HEXACO scale[57]. The trust and risk measures will serve as control variables when testing the primary (*a priori*) hypotheses (described in the next section), while the other variables will serve as moderators in further exploratory analyses.

On the day of the experiment, participants will arrive at the agreed upon time and meeting point. They will be escorted individually to a cubicle in the computer room, at which point they will be asked to sign the informed consent. They will not talk to anyone (except to the room supervisor, if necessary). To guarantee anonymity, their names will from then on be replaced by a self-made, retrievable code through which they can be identified during the remainder of the study.

Participants begin by filling out a 30-item multidimensional mood state (MDMS) questionnaire[58] and subsequently receive guidelines for spray administration. Participants will

then self-administer three puffs of the nasal spray in each nostril, and, following the procedures of Kosfeld et al.[8], wait 50 minutes before continuing with decision-making in the trust game. During this waiting period the procedures for the no-contact and the minimal social contact condition will differ (see Figure 1).

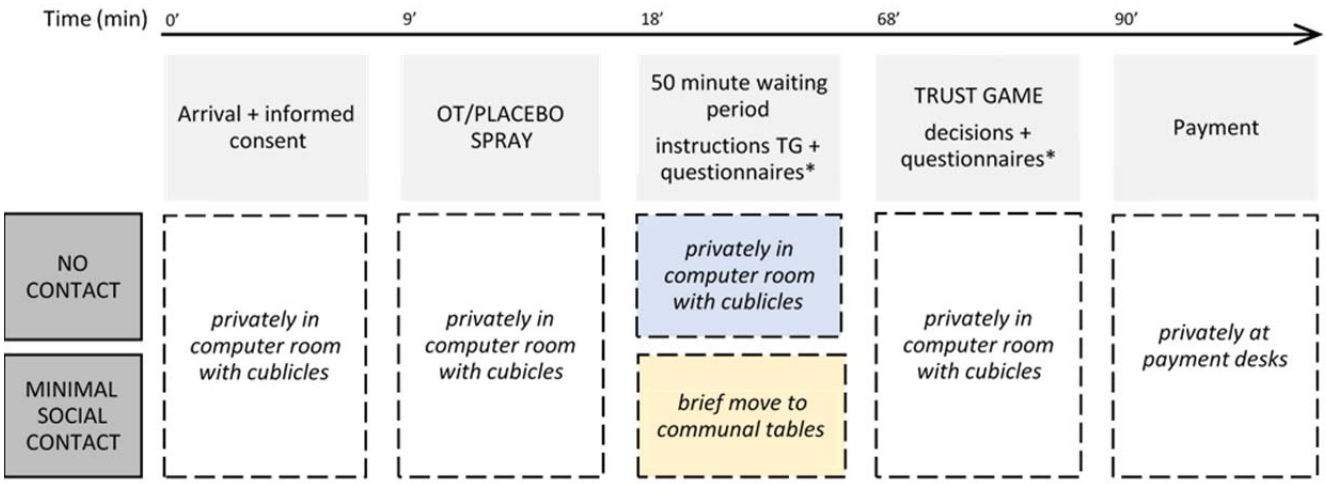

Figure 1. Condensed overview showing the main difference between the no-contact condition and the minimal social contact condition. The top arrow represents the time (in minutes) elapsed. The light grey boxes below describe the procedures, while the dotted-line boxes indicate where the experiment is taking place. The two experimental conditions differ only during the 50 minute waiting period. The questionnaires (indicated by *) are described in the text.

In the no-contact condition, participants will remain seated in their cubicles for the entire waiting period, and will fill out questionnaires that enable us to measure their negative reciprocity (Global Preferences Scale[55]), personality (the HEXACO-100 personality inventory[57]), fluid intelligence (Raven matrices task), and their level of arousal[59,60]. They will also fill out the MDMS questionnaire for a second time. This will enable us to check for mood changes

following nasal spray administration. During the last minutes of the waiting period, they will familiarize themselves with the trust game instructions.

In the minimal social contact condition, participants fill out the same questionnaires as in the no-contact condition. However, after 30 minutes into the waiting period, they will move together to a common room, where they will be seated at a communal table. They will be told that they have to sit here for roughly 8 minutes during which they fill out the MDMS and arousal questionnaires. They are told that they can talk quietly to each other, but they are not explicitly encouraged to do so. When they are done they will be guided back (as a group) to their respective cubicles, where they will receive the trust game instructions. From that moment on, the remainder of the experiment proceeds in the exact same way as in the no-contact condition.

The written instructions for the trust game will vary slightly between the no-contact and the minimal contact condition. In the no-contact condition, participants will read: *"During the study, you will be randomly matched with a participant from another room. Neither before, nor after the study will you learn the identity of the other participant. In the same way, the other participant will not be informed* about your identity." In the minimal social contact condition, participants will read: *"During the study, you will be randomly matched with one of the participants from the other room whom you just met. Neither before, nor after the study will you learn the exact identity of the other participant. In the same way, the other participant will not be informed about your identity."*

After concluding the experiment, participants will answer a post-experimental questionnaire. Importantly, this questionnaire will query participants' beliefs regarding the

387 treatment they received (OT versus placebo) which allows us to test the possibility of a placebo-
388 effect. Finally, a number of questions assess participants' feelings of connectedness with
389 others, which can be used to test if the *minimal social contact* and *no contact* condition differed
390 in this respect.
391 Participants are remunerated for their participation. They receive the earnings from the
392 decisions they made as described in the experimental instructions, plus a 5 euro compensation
393 for filling in the questionnaires.
394
395
396 **Data analysis**
397 *Hypothesis testing*
398 The dependent variable will be the investor's trust level in the various treatment conditions.
399 The main explanatory variables are the treatment conditions. We pool the data obtained in
400 Magdeburg and Antwerp because there is no a priori reason to expect that OT would affect
401 individuals from these two locations differently. In addition, pilot studies conducted during the
402 time span December 2017-March 2018 revealed very similar trusting behaviors between the
403 two locations (Supplementary Table 3a and Supplementary Figure 2). But to be on the safe side
404 we will still control for generalized trust[49] and general risk attitude[55] in our regressions. Adding
405 these two covariates will also reduce the standard errors in our treatment estimates – thus
406 allowing sharper estimates – and correct for potential imbalances in the samples that occur
407 through imperfect randomization. We do not plan to include social value orientation[48] as a
408 covariate because we control for SVO via stratified randomization. We will run the following

409 OLS-regression where T = Trust; OT = Oxytocin treatment; MSC = minimal social contact

410 condition; NoC = no contact condition):

$$T = \beta_o + \beta_1 OT + \beta_2 MSC + \beta_3 OT \times MSC + controls\ (generalized\ trust, risk\ attitude)$$

411 In this regression, the Placebo/NoC treatment is the omitted category and β_0 measures the

412 trust level in this treatment. Neglecting the covariates, the average trust levels in the four

413 treatments are given by the matrix in Table 1:

414

	Placebo (P)	Oxytocin (OT)
No Contact (NoC)	β_o	$\beta_o + \beta_1$
Minimal Social Contact (MSC)	$\beta_o + \beta_2$	$\beta_o + \beta_1 + \beta_2 + \beta_3$

415 **Table 1.** Regression coefficients estimating trust in each of the four experimental conditions
416

417 We test the following *a priori* hypotheses regarding the effect of OT and express them also in

418 terms of the coefficients of the above regression model:

419 **H1:** OT has a positive influence on trust in the MSC condition, i.e., $\beta_1 + \beta_3 > 0$. This is the

420 replication of the Kosfeld et al.[8] study, as delineated in finding (i) in the section on the

421 determination of the sample size.

422 **H2:** The influence of OT on trust in the MSC condition (which is given by $\beta_1 + \beta_3$), is higher than

423 the influence of OT on trust in the NoC condition (which is given by β_1), that is, $\beta_3 > 0$.

424 In addition we formulate a third hypothesis about the influence of the MSC condition:

425 **H3:** In the placebo treatment, Trust is higher in the MSC condition than the NoC condition, i.e.,

426 $\beta_2 > 0$.

As we do not have *a priori* expectations about the effect of OT in the NoC condition (i.e., whether $\beta_1>0$), we do not formulate a hypothesis. Similarly, although our design enables us to check whether the influence of MSC on trust levels in the OT treatment (which concerns $\beta_2 + \beta_3$) will be significantly different from zero, we consider this of secondary interest for the present study.

If the analysis yields a non-significant p-value, Bayesian hypothesis testing will be used to assess the relative evidence for the different hypothesis.[61] For example, a Bayesian analysis of H1 ($\beta_1 + \beta_3 > 0$) above computes whether the likelihood (L) of a model that captures the potential effect of OT (β_1) and the interaction effect between OT and MSC (β_3) is sufficiently more likely, given the data, than a model that assumes that both β_1 and β_3 are zero.

We will use the "regression BF" function in the Bayes Factor R package, using a JZS/Cauchy prior with a scaling constant of r=0.354, which corresponds to a prior with a medium width. We will also conduct robustness checks using larger values (r=0.5 and r=0.707) corresponding to wider and flatter prior distributions. For each hypothesis we test, we will compute a Bayes factor which provides an indication of how much more likely the hypothesized model is than the null model (i.e., no effect of Oxytocin on trust). We will consider a Bayes factor of 10 as sufficient evidence for the hypothesized model over the null model, a value that is considered "strong evidence" according to Jeffreys' classification system[62, 63].

The anonymized dataset generated and analyzed during the current study will be shared publicly.

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Author contributions

C.D., C.B., B.V. and E.F. developed the idea of a replication study that controls for minimal social contacts; C.D., C.B., B.V. and E.F. designed the study with contributions from L.P.; C.D., C.B., B.V. and E.F. wrote the preregistration report; C.D. and B.V. will supervise and conduct the data collection.

Competing interests

The authors declare no competing interests

Supplementary Information

Supplementary Table 1. A priori sample size computation using the G*Power 3.1.9.2 28 software[1]

t-tests: Difference between two independent means (two groups)		
Analysis	A priori: compute required sample size	
Input	Tail(s)	**One**
	Effect size d	**0.514**
	α error prob	**0.05**
	Power (1-β error prob)	**0.95**
	Allocation ration N2/N1	**1**
Output	Noncentrality parameter δ	**3.311**
	Critical t	**1.654**
	DF	**164**
	Sample size group 1	**83**
	Sample size group 2	**83**
	Total sample size	**166**
	Actual power	**0.951**

Supplementary Table 2. Simonsohn's small telescopes approach[2] to assess the adequacy of the sample size of a replication study. This method assesses whether the replication study has 80% power to detect an effect size the original study had 33% power to detect.

t-tests: Difference between two independent means (two groups)		
Analysis – Step 1	Compute required effect size for the Kosfeld et al.[3] study with 33 % power	
Input	Tail(s)	One
	α error prob	0.05
	Power (1-β error prob)	0.33
	Sample size group 1	29
	Sample size group 2	29
Output	Noncentrality parameter δ	1.220
	Critical t	1.672
	DF	56
	Effect size d	0.320
Analysis – Step 2	Compute required sample size using d = 0.32	
Input	Tail(s)	One
	Effect size d	0.320
	α error prob	0.05
	Power (1-β error prob)	0.80
	Allocation ration N2/N1	1
Output	Noncentrality parameter	2.502
	Critical t	1.651
	Sample size group 1	122
	Sample size group 2	122
	Total sample size	244
	Actual Power	0.802

Supplementary Table 3. Mean Investments in the Trust game across 11 pilot sessions

Supplementary Table 3 documents our effort to develop an experimental design that implements a trust game with and without a minimal social contact condition but which avoids introducing a ceiling effect for a potential impact of OT. For example, in experimental sessions 2, 5 and 7 below (which implemented the Social 1 condition or the Social 1* condition, for a detailed explanation of these conditions see text after Table S3) the average behavioral trust level was 8.875, 10.875 and 9.437, respectively. These trust levels are very high and leave little space for OT to have an effect in these conditions. Therefore, we conducted further pilots with a Social 2 and a Social 3 condition (see pilot sessions 9 – 11) which tried to mitigate these potential ceiling effects while still allowing for minimal social contact among the subjects.

#	DATE	Place	N	Condition	Stakes	Show-up fee	Gender	Invest options	Mean investment
1	15-Dec 2017	Antwerp	14	No contact	1pt = 33 c	5 €	mixed	all integers (0 – 12)	8.786
2	15-Dec 2017	Antwerp	16	Social 1	1pt = 33 c	5 €	mixed	all integers (0 – 12)	8.875
3	16-Jan 2018	Magdeburg	16	No contact	1pt = 1€	5 €	mixed	all integers (0 – 12)	7.313
4	17-Jan 2018	Magdeburg	16	No contact	1pt = 33 c	5 €	mixed	all integers (0 – 12)	8.813
5	17-Jan 2018	Magdeburg	16	Social 1*	1pt = 33 c	5 €	mixed*	all integers (0 – 12)	10.875
6	1-Feb 2018	Magdeburg	16	No contact	1pt = 1€	none	mixed	all integers (0 – 12)	6.936
7	1-Feb 2018	Magdeburg	16	Social 1	1pt = 1€	none	mixed	all integers (0 -12)	9.437
8	3-Mar 2018	Magdeburg	16	No contact	1pt = 1€	none	males	0, 4, 8, 12	8.250
9	3-Mar 2018	Magdeburg	16	Social 2	1pt = 1€	none	males	0, 4, 8, 12	7.500
10	16 Mar 2018	Magdeburg	16	Social 3	1pt = 1€	none	males	all integers (0 – 12)	8.100
11	16 Mar 2018	Magdeburg	16	Social 3	1pt = 1€	none	males	0, 4, 8, 12	8.000

The social conditions are defined as follows. In **Social 1**, after being seated and having signed the informed consent form in the experimental room, eight participants were called to meet each other briefly (5 minutes) in a smaller room (different from the experimental room where the trust game would be played). They were seated at the same table and then asked to formally introduce themselves by name, mention their hobby, and shake hands with each other, following the Prior Contact condition described in Declerck et al. (2010)[3]. In **Social 1*** (pilot session 5), the experimental rooms were separated by gender (i.e., men and women were not seated in the same room when they arrived or when they were performing the trust game). During the social contact moment, four males from one room met four females from another room and introduced themselves following the same procedures as in Social 1. This led to very high trust levels. In **Social 2** (pilot session 9), eight male participants met in the smaller room without introducing themselves. They were seated at the same table and waited together for 5 minutes during which they did not speak

with each other. This complete lack of verbal interaction caused a strange and akward situation that was associated with reduced investments. In **Social 3** (pilot session 10 and 11), we combined the procedures of Declerck et al (2010)[3] and Kosfeld et al. (2005)[4]: eight male participants, coming from 2 separate experimental rooms where the trust game was to be played, met in a smaller room. They were not asked to formally introduce themselves, but were told that they were permitted to talk, should they wish to do so. During the 8 minutes that they waited together, they were sitting at the same table and filled out questionnaires (see main text). These procedures were examined once with a "continuous" action space for the investor (i.e., investments from 0 – 12 were possible; in session 10) and once with a restricted investment space (only investments 0, 4, 8 and 12 were possible; session 11). Pilot session 8, which implements the no-contact condition, otherwise matches the procedures of session 11.

There were also the **following procedural differences** between the various pilot sessions. In **session 1 and 2** participants sat in computer rooms without cubicles; in all other session, participants sat in cubicles the entire time, except during the social contact manipulation in the non-experimental ("smaller") room. In **sessions 1-5** participants arrived at an agreed upon place where they waited together until the beginning of the experiment. In **sessions 6-11**, participants were guided immediately to their cubicles upon arrival. This minimizes the contact with other participants before the experiment and increases our control over subjects social contacts. The show up fee was removed in **sessions 6-11** for the following reason. We hypothesized that if subjects receive a show-up fee of €5 they are more willing to take social risks in the trust game, i.e., more willing to send their whole endowment of €12 in the trust game, which exacerbates the ceiling problem discussed above. Instead of giving them a show-up fee of €5 before the trust game we remunerated them ex-post with €5 for filling out questionnaires.

Supplementary Table 3b. Mean investments by gender in the mixed gender sessions 1-6

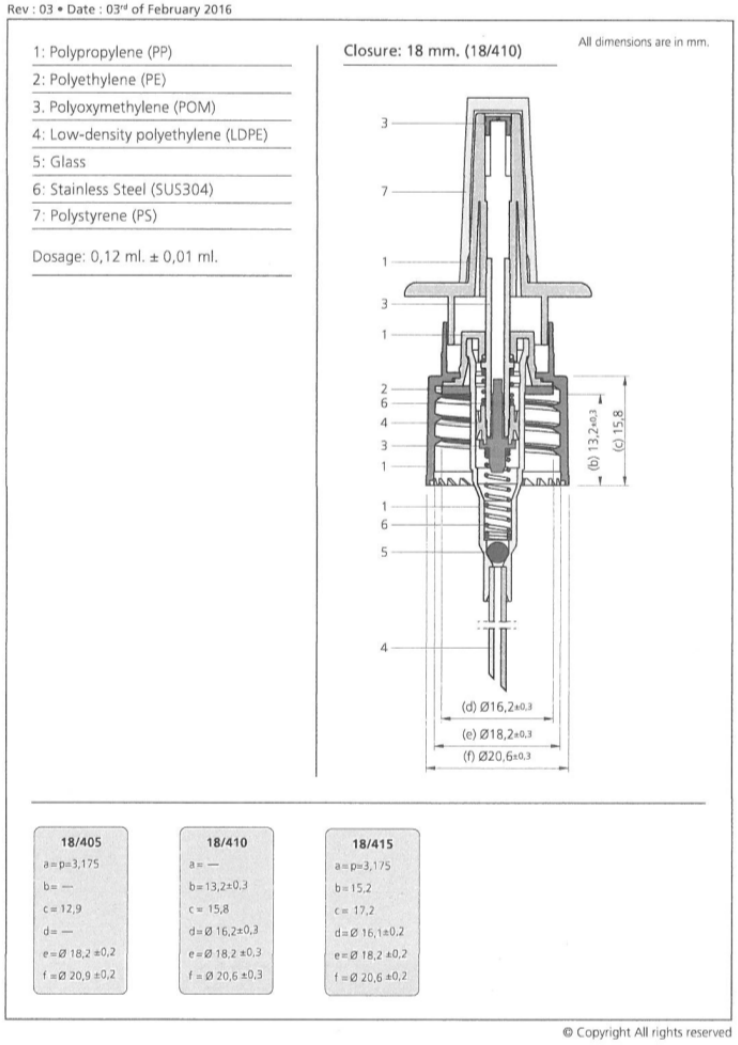
#	Condition	Mean all	Males	Females
1	No contact	8.786	10.6 (n=5)	7.8 (n=9)
2	Social 1	8.875	7.0 (n=10)	12.0 (n=6)
3	No contact	7.313	6.5 (n=8)	8.125 (n=8)
4	No contact	8.813	10.5 (n=8)	7.13 (n=8)
5	Social 1*	10.875	10.75 (n=8)	11 (n=8)
6	No contact	6.936	8.75 (n=8)	5.125 (n=8)
7	Social 1	9.437	9 (n=8)	9.875 (n=8)

The above table shows that in several of the first 6 sessions there were substantial gender differences in trust. To avoid this source of variation we decided to conduct the experiment with only male subjects.

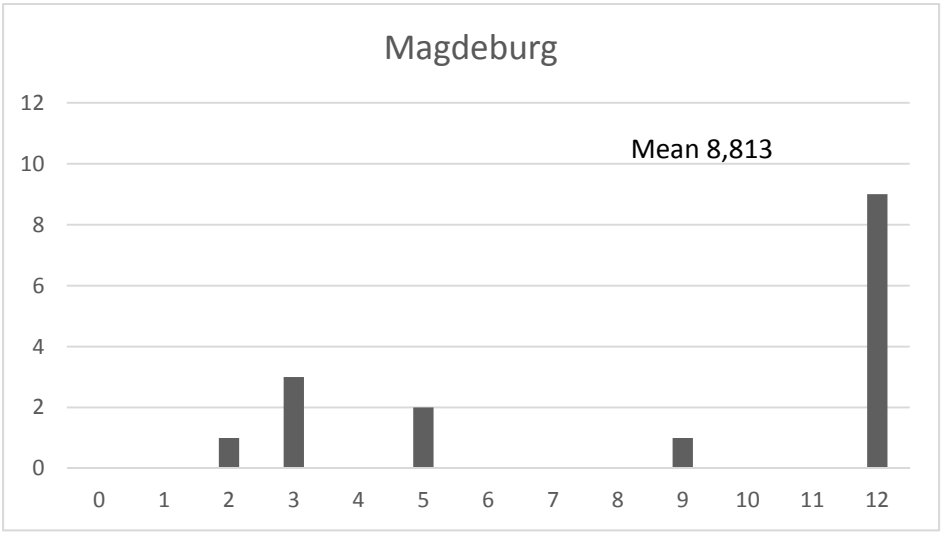
Supplementary Table 4. Guidelines for OT administration, based on recommendations by Guastella et al., 2013[5].

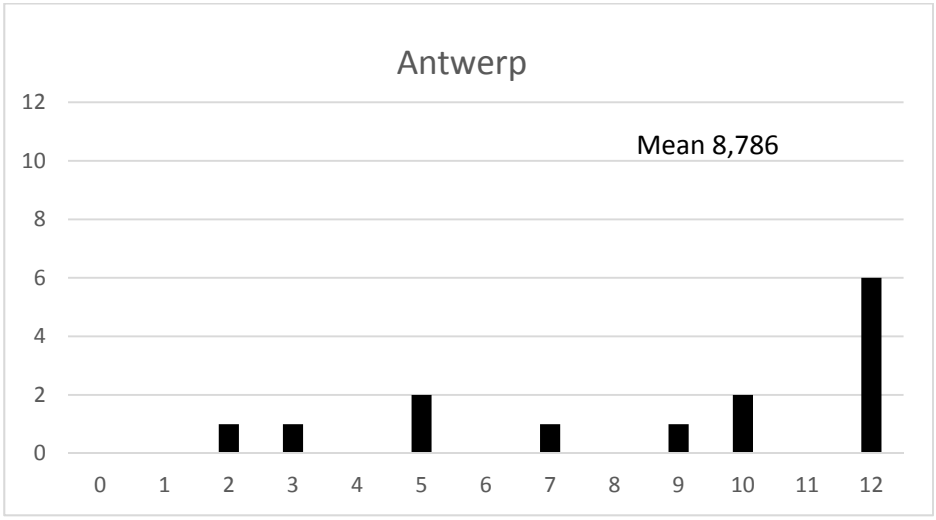
1	If necessary, clear your nose from any obstruction (box of tissues provided).
2	Prime the bottle and complete a test spray in the air.
3	Sit comfortably and keep the head in an upright position.
4	Close one nostril with one finger while administering the spray to the other nostril.
5	Insert bottle 1 cm into the nostril and keep the tip of the bottle at a 45 degree angle into the nose. Aim towards the upper lateral part of the nose (and not towards the middle of the nose).
6	Upon delivery, inhale and breathe in lightly. Do not sniff exaggeratedly.
7	Alternate administrations between nostrils. Allow time between each re-administration to the same nostril of at least 15 seconds.

Supplementary Figure 1. Technical details of finger sprayer used to deliver OT/placebo. Figure reproduced with permission from Pharma-pack, Wilrijk (Belgium).



Supplementary Figure 2. Comparison of the distributions of investment decisions in the pilot studies conducted in Antwerp (N = 14, session 1) and Magdeburg (N = 16, session 4). Experimental conditions are kept the same: no contact, mixed genders, low stakes (1 point = 33 cent) but with a show-up fee.





Supplementary References

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